Remarks

The present claims are claims 1, 3-5, 7 and 9-12. Favorable reconsideration of this application is respectfully requested.

Claim 1 has been amended to incorporate the subject matter of original claim 8. Claim 10 has been rewritten in independent form. In claim 10, the equation has been corrected by inserted the sigma (Σ) symbol to designate the sum of peak intensities. Additionally, independent claims 1 and 10 avoid the unnecessary terminology "without the use of calibration curves".

Applicant acknowledges election of Group I, original claims 1-15, with traverse. Nonelected claims 16-26 have been canceled without prejudice in favor of continuing prosecution.

Claims 1 and 13 were objected to based on certain terminology. Present independent claims 1 and 10 incorporate the alternate terminology suggested by the Examiner.

Claims 1-7 and 12 were rejected under 35 USC 112, first paragraph, as nonenabled. It is believed the present amendments obviate this rejection, or at least most aspects of this rejection, in that independent claim 1 incorporates the equation from original claim 8, and original claim 10 was not included in the rejection. However, the following comments are provided.

The equations recited in independent claims 1 and 10 do not need to be derived for each new protein or other sample analyte. The equations are based on physical properties of the sample analyte, like molecular weight and ionization potential. The equation in claim 1 can be used when the sample analyte and internal standard have similar ionization potential. In the equation recited in claim 10, the constant C takes into account the ionization potential of the sample analyte relative to the internal standard ionization potential.

The peak intensities are determined from the mass spectra, and the concentration of the internal standard is known. Thus, the only remaining unknown is the concentration of the sample analyte of interest. In other words, the equations are used to determine the concentration of the sample analyte, thus "quantitatively analyzing the sample analyte".

As mentioned C is the ionization potential of the sample analyte of interest relative to the internal standard ionization potential. If the C is not known for a new protein of interest, it can be determined via two approaches. First, protein chemistry determines ionization potential. So for positive MALDI mass spectra there are only a few chemistries that will positively charge in

the gas phase: metals, arginine, lysine and histidine. Therefore, based on this approach, there are four constants that are possible verses one internal standard. There is a "hierarchy" of ionization potential: 1)metals, 2)arginine, 3)lysine and 4)histidine. So if a protein sequence contains iron it will have one constant relative to one internal standard, arginine and no metals another constant, lysine and no metals or arginine, another constant, and so forth -- which means one can classify a protein analyte based on protein chemistry. The second approach is to isolate the unknown protein and perform one MALDI experiment with a known concentration versus an internal standard. Comparing the intensity ratios, molecular weight and concentration will determine the constant C. Under either approach, once C is established, the unknown amount of sample analyte can be quantified repeatedly at any concentration.

Regarding the specific objection to claim 3 regarding DNA, one can use the methodology discussed above, to determine the ionization potential, and then quantitatively determine the concentration in a sample. As a first example, if a DNA fragment is the sample analyte, a known DNA fragment having an assumed similar ionization potential can be used as the internal standard, in which case the equation in claim 1 may be used. As another example, the constant C can be determined by evaluating a known concentration of the sample analyte, such as in the second approach discussed above.

Claims 8 and 9 were rejected under 35 USC 112, first paragraph, as nonenabled. Additionally, claims 10 and 11 were rejected under 35 USC 112, first paragraph, as nonenabled.

While it is true that the examples in the specification employ certain solvents and matrices, it is not believed the claims need to be limited to recite such solvents and matrices. One skilled in the art could readily practice the invention by following the teachings of the specification – the enablement provisions of Section 112 require nothing more. There is no need for one to vary the solvents and matrices, i.e., one can practice the invention without doing so.

Regarding the aspect of this rejection relating to selection of internal standard, as pointed out above, it is not necessary that the sample analyte and internal standard have similar ionization potentials. In other words, if the sample analyte and internal standard have similar ionization potentials, then the equation recited in claim 1 can be used; if they don't have similar ionization potentials, then the equation recited in claim 10 can be used. Further, the specification teaches how to determine the C constant recited in claim 10.

Claims 1-12 were rejected under 35 USC 112, second paragraph, as indefinite. It is believed the objections raised for original claims 1, 2, 8, 10 and 11 have been addressed above.

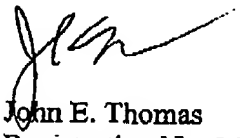
Claim 13 was rejected under 35 USC 102(b) as anticipated by Nelson et al. Claims 1-4, 7 and 12 were rejected under 35 USC 103(a) as unpatentable over Nelson et al. Claims 14-15 were rejected under 35 USC 103(a) as unpatentable over Nelson et al. in view of Kingshott et al. It is believed the present amendments obviate these rejections, noting that original claims 8 and 10 were not included in the rejections.

Finally, Applicant understands the comments regarding the layout of the specification are merely advisory and provision of a substitute specification is not required.

Attached hereto is a list of references. Copies of the literature references will be forwarded as soon as available to the undersigned.

The Examiner is invited to contact the undersigned to resolve any remaining issues.

Respectfully submitted,



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